Large-Scale Clonal Analysis Resolves Aging of the Mouse Hematopoietic Stem Cell Compartment.

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Public Summary:
Stem cells are responsible for replenishing tissues throughout life. However, aging within the stem cell population can result in loss of tissue regeneration and underlie the gross consequences of physiological aging. Here, we have investigated tissue stem cell aging within the blood system of mice. We used single cell approaches to determine how the blood stem cell compartment changes with age. We identified large changes in stem cell function with age as well as a novel stem cell population specific to the aged bone marrow. These findings are informing our understanding of how tissue stem cells age and efforts to rejuvenate blood system function in the elderly.

Scientific Abstract:
Aging is linked to functional deterioration and hematological diseases. The hematopoietic system is maintained by hematopoietic stem cells (HSCs), and dysfunction within the HSC compartment is thought to be a key mechanism underlying age-related hematopoietic perturbations. Using single-cell transplantation assays with five blood-lineage analysis, we previously identified myeloid-restricted repopulating progenitors (MyRPs) within the phenotypic HSC compartment in young mice. Here, we determined the age-related functional changes to the HSC compartment using over 400 single-cell transplantation assays. Notably, MyRP frequency increased dramatically with age, while multipotent HSCs expanded modestly within the bone marrow. We also identified a subset of functional cells that were myeloid restricted in primary recipients but displayed multipotent (five blood-lineage) output in secondary recipients. We have termed this cell type latent-HSCs, which appear exclusive to the aged HSC compartment. These results question the traditional dogma of HSC aging and our current approaches to assay and define HSCs.